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STROKES—DIAGNOSIS AND MODERN TREATMENT: I. DIAGNOSIS*†

Most strokes, like myocardial infarctions, represent chapters in the natural history of atherosclerosis or of thrombosing or hemorrhagic diseases. It is by a turn of fate that brain involvement occurs instead of the heart or kidneys. Within one year, 50 per cent of patients with a thromboembolic stroke who have not received anticoagulant therapy will develop additional thromboembolic complications somewhere in the body. Twenty-five per cent will develop a cerebral thromboembolism. By the fourth year, these figures reach 90 and 40 per cent,[1] respectively. Therefore, a sound approach to this problem necessitates the broad view and a study of many pathogenic and therapeutic facets.[2]

Strokes may develop from a variety of conditions, many of which are rare. These are comprehensively listed in "Classification and Outline of Cerebrovascular Diseases."[3] This discussion will deal with the three most common causes of strokes: thrombosis (usually superimposed on atherosclerosis), embolism (most commonly secondary to heart disease with an irregular rhythm) and hemorrhage (usually secondary to a weakened vessel wall due to atherosclerosis, a congenital malformation, or to a blood dyscrasia). The differential diagnosis and modern treatment of each will be outlined.

These conditions should be considered from different viewpoints in order to answer the following questions:

1. Is the stroke under study due to a thrombosis, embolism, or hemorrhage, or is it a temporary manifestation due to vascular spasm or sludge in a narrowed vessel?

2. Is this due to occlusion of the carotid arterial system, the basilar-vertebral arterial system, or a smaller branch more peripheral in the tissue or on the surface of the brain?

3. Is a single major or minor vessel involved, or is the condition the result of numerous "little strokes" which have produced widespread diffuse damage?

4. What brain centers have been damaged and to what degree?

The following schema (Table I) is offered to help the clinician answer some of these questions, but even with its aid they will often tax his best efforts.

From the viewpoint of anticoagulant therapy, this differential diagnosis is fundamental. Cerebral infarctions due to emboli and, to a lesser degree, thrombi, are often associated with hemorrhage into the brain tissue, not always revealed in the spinal fluid. Experimental embolic infarcts have yielded conflicting results regarding the risk of hemorrhage from anticoagulant therapy.[4,5] Clinical experience, however, thus far has indicated that even though the possibility of hemorrhagic infarction exists, the outlook following cerebral embolism, both immediate[6] and long-term,[1] has been markedly improved by anticoagulant therapy.

The differential diagnosis between involvement of cerebral arteries, the carotid and the basilar-vertebral arterial systems has been studied in detail by Fisher,[7] Dunning,[8,9] and Millikan, Siekert and Shick.[10,11]

Cerebral Arteries

Thrombosis of a cerebral artery frequently occurs during sleep or shortly after arising in the morning. A careful history will often reveal that in the past the patient has suffered from transient, similar episodes to which little attention has been paid. It is important to be alert to these first signs, such as slight difficulty or slurring of speech, weakness of the facial muscles, numbness and weakness of the hands or legs which may last only a few minutes, or an hour or so. They are warning signals and today something can often be done to forestall further developments.

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† Part II of this article, concerned with the treatment of strokes, will follow in the May issue.

At the onset of the attack, the patient may suffer from headaches. The spinal fluid should be examined. With this type of stroke it is usually normal, although occasionally the protein may be increased but seldom as high as 100 mg. per cent. It is essential to determine whether there is xanthochromia or blood in the spinal fluid. Their absence does not rule out the possibility of hemorrhages, which may be deeply imbedded in brain tissue. Typical neurological signs indicating involvement of the middle cerebral artery include contralateral hemiplegia with cortical sensory deficit and hemianopia. If the occlusion is on the dominant side of the brain, aphasia may occur and if the resulting infarction is massive, stupor. The extent of the damage depends on whether a small branch of the artery supplying the peripheral areas of the brain is at fault, or whether, for example, the deep territory of the middle cerebral artery is affected. The latter would include the upper part of the posterior limb of the internal capsule and the adjacent basal ganglia, in which case the face, arm and leg might be involved at the same time. If the anterior cerebral artery is occluded, the typical findings include paralysis and corticohypesthesia of the opposite lower limb and possibly mild similar changes in the opposite arm. Mental changes, often described as dementia, grasping and sucking reflexes and incontinence of the bowel and bladder may be seen. The syndrome associated with a block of the posterior cerebral artery depends upon the site of obstruction. There may be some mental changes and mild contralateral hemiparesis. Bilateral posterior cerebral involvement, in which both occipital lobes are affected, may result in cortical blindness. The patient is frequently unaware that he cannot see.

Carotid Arteries

Gradual occlusion of the internal carotid artery may be symptomatic for a period of months or even years before the final occlusion occurs. The clinical picture temporarily may resemble that of the middle cerebral artery as outlined above. However, a rather characteristic sign of occlusion of the internal carotid artery is monocular blindness, which may be fleeting or permanent, and involves the eye contralateral to the hemiplegia. This results from interference of the blood flow of the ophthalmic artery, one of the branches of the internal carotid. Dunning[8, 9] has emphasized the importance of the absence of pulsations of the carotid arteries, when determined by pharyngeal palpation, as a diagnostic sign of occlusion. This is not always easy, but it is significant if the opposite carotid can be felt easily.

Table I

Differential Diagnosis of Cerebral Thrombosis, Cerebral Embolus and Intracerebral Hemorrhage

Incidence	Cerebral Thrombosis (70-80 Per Cent)	Cerebral Embolus (5-22 Per Cent)	Cerebral Hemorrhage (8-15 Per Cent)
Age groups	Same as for hemorrhage	As majority of cases occur from rheumatic hearts, most patients are young adults or early middle-aged	Same as for arteriosclerosis (increasing with each decade over 50)
History and general physical examination	Same as for hemorrhage, but blood pressure normal in majority of cases; may be elevated	Rheumatic heart disease with mitral stenosis; bacterial endocarditis; auricular fibrillation; recent myocardial infarction; emboli elsewhere, as in lungs, arms, legs, kidneys, or mesentery; usually at least one of these pathological states can be found	Evidence of arteriosclerosis in retinal or peripheral vessels or other evidence of disease of cardiovascular system; blood pressure often elevated; the systolic pressure usually above 200 mm. Hg
Onset	Difficulty in speaking and weakness of arm or leg are the usual first symptoms; onset may be gradual or sudden	Very sudden, abrupt development of neurological signs	Severe headache, nausea and vomiting frequently occur at onset, followed by coma

Table I (Continued)

Differential Diagnosis of Cerebral Thrombosis, Cerebral Embolus and Intracerebral Hemorrhage

Incidence	Cerebral Thrombosis (70-80 Per Cent)	Cerebral Embolus (5-22 Per Cent)	Cerebral Hemorrhage (8-15 Per Cent)
Coma	Often none at all; if present, usually less than 24 hours	Coma not usual, unless embolus is large	If coma persists more than 24 hours, hemorrhage more likely
Convulsions	Occur in 7 per cent of patients at onset	May occur	Occur in 14 per cent of patients at onset
Cheyne-Stokes or labored respiration	Seldom	Rare	Common
Conjugate deviation of eyes	Seldom	Rare	Frequent
Quadriplegia	Rare except in thrombosis of basilar artery	Rare	Rare
Stiff neck	Rare	Rare	Frequent
Bilateral extensor plantar response (positive Babinski)	Rare	Rare	Frequent
Leukocytosis	Uncommon	Uncommon unless embolus is infected	More than 50 per cent of patients have over 12,000 leukocytes per cu. mm.; often greater than 20,000
Cerebrospinal fluid	Fluid usually clear, pressure slightly increased, but not above 250 cm. of water There may be slight pleocytosis and an increase in protein content	Fluid may be clear or xanthochromic There may be a moderate pleocytosis and increase in protein content, especially if embolus is septic	Usually bloody and under increased pressure Bloody fluid diagnostic of hemorrhage into ventricular or subarachnoid space Fluid xanthochromic if hemorrhage is old; rarely may be clear if hemorrhage is deep in brain tissue or walled off

Basilar-Vertebral System

Usually the two vertebral arteries are of fair size. Such being the case, unilateral occlusion of one may give no demonstrable clinical signs, or it may cause the syndrome of the posterior inferior cerebellar artery. This may be characterized by facial pain, vertigo, vomiting, dysphagia, ataxia, Horner's syndrome, contralateral loss of sensation of pain and temperature on the extremities and tongue, and homolateral involvement of the face. When there is only one vertebral artery of substantial size, and it becomes

occluded, the basilar artery syndrome is produced. The basilar artery supplies the pons and usually the territory of the posterior cerebral arteries, which includes the midbrain, thalamus and temporo-occipital portion of the cerebral hemisphere. Occlusion of this vessel produces bilateral pyramidal tract signs, combined with unilateral and bilateral cranial nerve palsies involving the third to the eleventh nerves. This may produce weakness or paralysis of all four limbs, with increased tendon reflexes and bilateral Babinski signs, dysphagia, diplopia, dysarthria, numbness of the face, weakness of the masseter muscle, stupor or coma, and, rarely, unilateral or bilateral deafness. Frequently, there is noted also rotational vertigo, cerebral ataxia, and long tract sensory deficit, with visual field defects or blindness. *It is quite characteristic in basilar artery occlusion* for the patient to have had intermittent symptoms for months or even years before a final attack, and *for these symptoms to have changed from one side to the other.* In other words, one minor attack may affect the left side of the body, the second the right, and these signs may vary markedly in their expression. It was not uncommon in the past for these patients to be thought to be neurotic because of the variability and complexity of their complaints.

Cerebral Embolism

The signs produced by a cerebral embolism depend upon where the embolus lodges, how large is the area of infarction, whether the embolus propagates and blocks off additional arterial branches, how much blood leaks into the infarcted area and various other factors. Here the clinician is confronted not only with the problem of the local pathology secondary to the embolus, but also with the treatment of the source of the embolus. This is usually located in the left side of the heart, but may be found in the aorta or carotid arteries. More rarely it may be in the vertebral or basilar arteries or in an aneurysm of any of these vessels. More often than not, auricular fibrillation will be present, either on the basis of rheumatic or arteriosclerotic heart disease. Emboli also may arise from hearts affected by long-standing rheumatic damage with normal sinus rhythm. Thrombi secondary to bacterial endocarditis can give rise to septic emboli, which may produce a local and sometimes a gradually spreading infection within the brain. Spinal fluid abnormalities may point to this complication. Emboli may arise from surgery of the lungs involving the pulmonary veins, surgery of the neck and thorax, and fairly frequently after cardiac surgery such as that for mitral stenosis. After fractures, fat emboli usually lodge in the pulmonary circuit.

Recently, the phenomenon of transient cerebral ischemia without infarction has been subjected to more careful scrutiny, particularly by Dr. Millikan of the Mayo Clinic.[10,11] Dr. Miller Fisher, of Massachusetts General Hospital,[7] and on our own service at the New York Hospital—Cornell Medical Center. The question as to whether such transient episodes can be produced by vasospasm is still not settled in the minds of many neurologists and internists. It is our own opinion that such phenomena can and do occur. Vasospasm can be observed in arteries and arterioles in many other areas of the body. It is frequently seen in the vessels of the brain during neurosurgical procedures. It seems logical, therefore, to conclude that cerebral vasospasm may result from a variety of changes that cause sufficient stimulation or irritation of the neurovascular mechanism. Whatever their mechanism, these transient episodes should not be regarded lightly, since they are frequently a warning sign, presaging a later serious cerebrovascular stroke. This is particularly true if the carotid and basilar arteries are involved, but also may be so in the cerebral artery areas. The transient stroke often presents a miniature of what the patient later develops. Except for the basilar artery manifestations, these recurrent signs and symptoms usually will be fairly consistent. Such attacks may last a few seconds or an hour or two. They may be few or many in number and may even recur over a period of several years. Formerly, there was nothing which could be done to prevent these recurrences. While their mechanism may be on the basis of vasospasm, as suggested above, perhaps more often it is due to a combination of atherosclerotic narrowing of the lumen with a temporary sludging of the formed elements of the blood, which then disintegrate and move on to clear the passageway and improve the circulation. Doubtless, in some cases, both factors operate; in others, the exact mechanism cannot be determined, even at autopsy. What is most important is that the use of anticoagulants will, in many patients, abolish these attacks.[4-7] This strongly suggests that soft thrombi play an important role in the production of these phenomena.

Hemorrhagic Strokes

Hemorrhage presents an even more difficult problem, since to date no satisfactory therapy has been developed to combat it. Intracranial hemorrhage accounts for about 25 per cent of cerebrovascular lesions found at postmortem examination. It is most commonly associated with high blood pressure, which is frequently, although not necessarily, extreme. At the time of the stroke, the systolic pressure, which formerly might have ranged from 180 to 230 mm. Hg, may rise as high as 275 or 280 mm. Hg, with or without a corresponding rise in the diastolic pressure. The exact explanation of this usually is not clear. Within a few days, this high pressure usually subsides to its former level, or even lower.

In the case of thrombosis, the patient frequently suffers his stroke while lying quietly in bed. These conditions tend to encourage stasis of the blood. On the other hand, the majority of patients who develop cerebral hemorrhage are up and about and active at the time, indulging, in some cases, in fairly strenuous activities or subjected to intense emotional strain. Usually these strokes come on without warning, except in cases where there has been slight leakage from a congenital aneurysm. They are apt to be violent and frequently cause widespread damage.

While hemorrhagic strokes are usually fairly massive affairs, it should not be assumed that all hemorrhagic strokes are fatal or even large. Many autopsies show evidence of an infinite number of small hemorrhages which have occurred in the recent or distant past, leaving minute scars, without the patient or his physician having been aware that this has taken place. Most spontaneous hemorrhages occur intracerebrally. Rupture of the arteries in the subarachnoid space is rare, apart from those arising from saccular aneurysms. Hypertensive hemorrhage infrequently occurs from the large arteries at the base of the brain. As the hemorrhage continues, a massive clot forms and extends. This displaces and compresses brain tissue and may compromise vital central structures. Frequently, rupture or seepage into the ventricular system occurs and the spinal fluid becomes bloody. However, if the hemorrhage is small or deeply placed in the brain tissue, the spinal fluid may remain clear on repeated examination. This presents a major problem in relation to anticoagulant therapy. This situation is the exception, however, and red blood cells or xanthochromia are found in the spinal fluid with the majority of intracerebral hemorrhages.

The rupture of the vessel may be due to a split in an atherosclerotic plaque, but hemorrhages may arise from vessels in which there is no ascertainable degree of atherosclerosis. They may develop from saccular aneurysms which are frequently small and thin-walled. These are most often seen in arteries of the circle of Willis, or the vessels which arise from that area. These aneurysms increase in frequency with age, and death occurs most commonly in the ages between 35 and 65. Since they are found with increasing frequency in aging, probably most of them are not purely congenital, but develop in the course of time because of an underlying congenital defect in the arterial wall.

Symptoms of hemorrhage from these, as with other types of hemorrhage, depend upon the location and degree of the hemorrhage. In addition to the localizing signs described above in relation to thrombosis, rigidity of the neck is very common, together with evidences of intracranial pressure, including edema of the discs, marked headache, and, not infrequently, evidence of retinal hemorrhage. Progressive or sudden blindness may occur from rupture of an aneurysm of the internal carotid or anterior cerebral artery. Convulsive seizures are not uncommon. The patient may survive the first attack but suffer a recurrence within days, weeks or months. The prognosis is poor. Surgery for these aneurysms and their complications has met with occasional success, but so far this therapy is in a developmental phase.

Arteriography

Arteriography, using the injection of radiopaque substances into the carotid system, has become an increasingly important tool in the diagnosis of intracranial lesions. The newer contrast agents and better techniques have resulted in fewer complications and it is now possible to identify lesions with this procedure which might otherwise be confused with thromboses. These include vascular and other tumors, arteriovenous anastomoses, expanding aneurysms, and spontaneous or traumatic hemorrhage. Where this technique is available, it should be used selectively, especially as a preliminary study prior to surgery.

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Proceedings of the Council for High Blood Pressure Research
American Heart Association, November, 1958

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